Morriss, Richard and Lobban, Fiona and Riste, Lisa and Davies, Linda and Holland, Fiona and Long, Rita and Lykomitrou, Georgia and Peters, Sarah and Roberts, Christopher and Robinson, Heather and Jones, Steven (2016) Clinical effectiveness and acceptability of structured group psychoeducation versus optimised unstructured peer support for patients with remitted bipolar disorder (PARADES): a pragmatic, multicentre, observer-blind, randomised controlled superiority trial. The Lancet Psychiatry . ISSN 2215-0374

Clinical effectiveness and acceptability of structured group psychoeducation versus optimised unstructured group support for remitted bipolar disorder: a multi-centre pragmatic randomised controlled trial.

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Summary

Background: Group psychoeducation (PEd) is a cheap NICE recommended treatment for bipolar disorder. Its clinical effectiveness and acceptability are unclear compared to unstructured group support (PS) matched for delivery and aim of treatment, and previous bipolar history.
Methods: Randomised, parallel group, observer blinded superiority controlled trial recruiting at eight sites from secondary care or self-referral with two year follow up. Participants aged 18 years or over with bipolar disorder, no episode in the preceding four weeks. Randomisation using minimisation for number of previous episodes (1-7, 8-19, 20+ bands) and site by clinical trials unit to either 21 two-hour weekly sessions of PEd or PS, allocation conveyed to trial co-ordinator and masking of assessors to outcome. Intention to treat primary outcome was time to the next bipolar episode with planned moderator analysis of number of previous bipolar episodes and qualitative interview of participant experience. Trial registration number ISRCTN62761948, ended.
Findings: From September 2009 to June 2012, 153 and 151 participants were recruited to PEd and PS respectively with complete primary outcome data. Fewer drop outs from treatment occurred in PEd versus PS (median (IQR) 14 (15.5) versus 9 (15) sessions, p=0.026). Over 96 weeks, time to first bipolar episode did not differ between PEd and PS (number of bipolar episodes 89 (58%) versus 95 (65%), hazard ratio (HR) = 0.83 (95% CI 0.62-1.11) p=0.217. The treatment was moderated in favour of PEd for participants with fewer previous bipolar episodes (X^2 = 6.80, p = 0.034, HR 0.28 (95% CI 0.12- 0.68) for 1-7 previous episodes). Four participants (1 PEd, 3 PS) died in the follow-up period of the study.
Interpretation: Structured group psychoeducation was no more clinically effective than similarly intensive unstructured group support but was more acceptable and improved outcome in participants with few previous episodes.

296 words

Introduction.

Bipolar disorder (BD) is a common relapsing life-long mental health condition presenting in adolescence or early adulthood (1). Worldwide it is 18th in years lived with disability of all health conditions (2) and associated with a 20-fold increase in suicide and two-fold increase in mortality from ischaemic heart disease (3). The provision of information and emotional support is a National Institute for Health and Care Excellence (NICE) supported key recommendation and quality standard for all mental health service users (4). In the United Kingdom, such information and support is widely available to people with bipolar disorder through unstructured peer run groups by both the NHS or the third sector e.g. over 130 national support groups through Bipolar UK (5). However, across Europe including the United Kingdom, such information and support for people with bipolar disorder has also been provided through structured group psychoeducation in mental health services (6, 7).

In 2003, researchers from Barcelona published two randomised controls (RCTs) of 21 session structured manualised group psychoeducation for people with bipolar disorder showing clinically important differences in time to all types of bipolar relapse at 12 and 24 months compared to attentional control support groups (8, 9). Their results influenced clinical practice because group psychoeducation had broad clinical effectiveness against relapse (10,11), as well as being helpful in improving knowledge, confidence and providing support to people with bipolar disorder (6,7). Hence group psychoeducation is a key recommendation by NICE in its clinical guideline for bipolar disorder and a national development quality standard (1). It is a cheap, efficient and easy to deliver easy- to-set- up option for mental health services because 10-18 participants can be treated at a time and therapists require supervision but not the extensive training required for other psychological treatments recommended for bipolar disorder. However, recently doubt has been expressed as to whether group psychoeducation, or indeed other psychological treatments, are really effective against bipolar relapse (12, 13). A recent meta-analysis of the effectiveness of psychoeducation on bipolar relapse noted that the original Barcelona trials (8. 9) seemed to be outliers compared to other RCTs of individual or group psychoeducation versus either treatment as usual or attentional controls (14). The evidence was reported as weak or very weak with few pre-registered large multicentre blinded RCTs conducted independently of the developers of the intervention (1, 14, 15). Few studies controlled for the variation in outcome due to natural history of bipolar disorder e.g. people with 20 or more previous bipolar episodes relapse three times more frequently than those with only 1-7 previous bipolar episodes (16).

The aims of our current randomised controlled trial were to independently examine:

1. The clinical effectiveness of structured group psychoeducation (PEd) versus unstructured group support (PS) on time to the next bipolar episode, including the moderating effects of number previous bipolar episodes, plus secondary outcomes in groups matched for the duration, delivery and aim of treatment, and previous bipolar history.
2. The experience, acceptability and subjective value of both treatments based on systematic qualitative enquiry and attendance at group sessions.

Methods.

Study design.

This is a randomised, parallel group, interviewer blinded, superiority controlled trial with two year follow up of each participant. Recruitment occurred at eight sites by self-referral or secondary mental health care. The study was conducted in the community in two regions of England (the North West and East Midlands). At three sites recruitment occurred at two separate time periods so recruitment

occurred in 11 waves (appendix, Figure A1). Ethics approval was obtained from a national ethics committee in Nottingham. The study protocol was published (17 and the statistical analysis plan is available on line at https://dx.doi.org/10.6084/m9.figshare.3205738).

Participants.
The recruitment strategy was deliberately broad to ensure that the sample reflected a diversity of people with BD. Community mental health teams at NHS Trusts at each site were encouraged to invite potentially relevant participants. The study was also promoted at a primary care level, with local family doctors being asked to display posters about the trial, and through service user-run local BD groups, national BD publications and the general media, allowing people to self-refer. The target population was patients with bipolar 1 or 2 affective disorder at increased risk of further relapse (defined as having had an episode in the last 24 months), as preventing relapse is the key aim of the intervention.

Participants were included if they:
- had a SCID-DSM-IV verified diagnosis of primary bipolar 1 or bipolar 2 disorder (18, 19),
- were at increased risk of relapse (at least one episode in the last 24 months),
- were aged 18 years or more

Participants were excluded if they had any of the following:
- presence of a manic, hypomanic, mixed affective or major depressive episode currently or within the previous four weeks,
- current suicide plans or high suicide intent,
- inability or unwillingness to give written informed consent to the study,
- inability to communicate in written and verbal English to a sufficient level to allow them to complete the measures and take part in the groups.

Randomisation and masking.
Consecutive eligible patients were individually randomised by a clinical trials unit to either intervention, using a stochastic minimisation software. Randomisation was stratified by clinical site and minimised within site by number of previous bipolar episodes within three categories (1-7, 8-19, 20 or more previous bipolar episodes, determined by SCID-DSM-IV criteria for past mania, hypomania, mixed affective or major depression episodes). At each site, recruitment continued until there was a minimum of 20 and a maximum of 36 participants per wave (see appendix figure 1a). Research assistants at each site enrolled participants. To ensure blindness of assessment the research assistants sent participants details to the trial co-ordination team (trial administrator and trial co-ordinator) at a separate site. Upon consent, the trial co-ordination team passed the participant information to the clinical trials unit for randomisation. The clinical trials unit reported the randomisation allocation to the trial co-ordination team which directly informed each participant and the lead health professional running the treatment group the participant was allocated to.

Masking of randomisation allocation was achieved by blinding the research assistants who recruited the participants at baseline and conducted follow ups. This was achieved by the following processes

1. Research assessors were based separately from the trial co-ordinator and trial administrator and all treatment groups.
2. Treatment groups were run identically (over the same time period, frequency, duration of sessions, base, both groups received a manual and led by the same health professional), to mask the day on which each group was run at each site,

3. All follow up data collected by self-complete questionnaire which could unblind the research assessor was returned in a sealed envelope to the research assistant carrying out the assessment and conveyed to the trial office for opening and subsequent data entry by another person.

Unblindings were recorded and if they occurred, all subsequent follow up assessments were conducted by another research assistant who was masked to treatment allocation. At baseline, before attending either group, participants were asked whether they had a preference for PEd, PS or no preference; all participants indicated they were prepared to attend either group.

Intervention procedures.

In both the PEd and PS groups, participants were told when they consented to the study and at the first and subsequent sessions that the purpose of this intervention was to share experiences to help manage BD using: i) the information given by the group facilitators, ii) their own experience, and iii) the collective experience of the group. The groups differed only in the structure, nature of delivery within the sessions, choice of content and type of content. The PEd group followed a curriculum developed in Spain (8, 9) (appendix, Table A1) but contextualised to English current practice by the research team and a panel of service users recruited for the purpose. The PS group set their own agenda and chose the content of their own programme (appendix, Table A2).

Both PEd and PS groups were run by three facilitators, comprising two health professionals (usually one experienced and one trainee facilitator) and a service user-facilitator with a diagnosis of BD. The facilitators were specially trained for the purpose and supervised by a psychiatrist (RM) or clinical psychologist (FL or SJ) experienced in delivering psychological treatment for bipolar disorder. However, none of the research team had devised PEd or PS nor had anything to gain from favouring either intervention allowing a completely independent trial. Service user facilitators were also offered additional peer support. Both programmes comprised 21 sessions, delivered once per week for two hours, spread over a maximum of 26 weeks (8, 9). The group sessions comprised a closed group starting with a minimum of 10 and a maximum of 18 participants to capture a variety of service user experience about the topics of every session. The sessions were held at the same community based site away from hospital e.g. day centre for both PE and PS contemporaneously on different afternoons of the week. A manual was produced for both PEd (20 adapted by authors) and PS on the aims and conduct of each group (available from authors). Participants in PEd were encouraged to share their staying well plan with their health professionals e.g. community psychiatric nurse, psychiatrist, general practitioner; and other people who were personally important to them. They were discouraged from sharing any information about the content of the group with other service users with bipolar disorder until their follow up was complete. In both trial arms participants received the trial group therapies in addition to their usual treatment. They were discouraged from attending any other course of group, family or individual psychological treatment for BD at the same time as attending the groups in the study. Otherwise treatment as usual was unconstrained and recorded by interview and from case notes.

The PEd group was run as a collaborative workshop with a brief taught introduction of the topic for the session, and the rest of the work taking the form of active interaction using the collective experience of the participants (8, 9). Embedded in the PEd programme is the acquisition of specific skills by each individual, including life charting, recognition of early warning signs, problem solving and other forms of coping, sleep hygiene and care planning, as well as general skills of actively participating and working collaboratively in the groups. They were encouraged and supported to

develop a plan that fitted their personalised goals for recovery and have two elements: (i) those actions they take every day to stay well, such as taking medication and keeping a regular early morning routine; and (ii) those actions they would take if they started to become unwell with mania or depression.

In the PS group, participants collectively decided upon an agenda for discussion at each session. The three facilitators were present to facilitate discussion, encourage participation, prevent unhelpful group behaviour such as bullying or scapegoating, prevent factual misinformation, and if directly asked to, clear up factual uncertainty. Compared to group support delivered routinely by Bipolar UK, PS was optimised by being closed to new participants so that they got to know each other well and it was facilitated by both a peer service user and two health professionals allowing the delivery of expert information from health professionals if participants requested it.

Treatment fidelity.
Treatment fidelity was maintained by training and supervision, written record of the content and delivery of the sessions completed by therapists and supervisors, and qualitative interviews with participants. Audiotaping and videotaping of sessions were not employed because some participants reported that they would find such recording intrusive and unacceptable.

Outcomes.
The primary outcome measure was time to next bipolar episode (17, 19) recorded by research assistants at each site. This was based on the SCID-LIFE (19, 21), carried out every 16 weeks for 96 weeks. We calculated time from randomisation to the first week of recurrence of an episode of mania, hypomania, a mixed episode, or major depression that lasted two consecutive weeks, satisfying DSM-IV criteria. When a follow up interview was not conducted, a bipolar episode was recorded when there was: (i) a description of symptoms of a manic or depression type episode, in primary or secondary care mental health records, with symptoms of sufficient duration to meet episode criteria (17, 22) and (ii) there was a change of medication, care setting (inpatient or crisis team) or urgency of being reviewed because of these symptoms.

Secondary outcome measures (17) were:
- time to next mania-type episode (mania, hypomania or mixed affective episode) and time to next depressive episode (19, 22);
- assessment of mean weekly symptoms of mania type symptoms and depression symptoms using the LIFE (19, 22);
- assessment of function using the Social Adjustment Scale (SAS) (23) and SOFAS (24);
- observer and self-rated measures of mood: 17 item Hamilton-GRID (HDRS) (25), Bech-Raphaelson Mania Scale (MAS) (26), Hospital Anxiety and Depression Scale (HAD) (27);
- self-rated overall mental and physical health (SF-12 mental and physical component scores) (28)
- the EQ-5D 3L (29) was used to assess health status;

At each assessment, suicide, neglect and risk were recorded in addition to other assessments. We recorded the type and amount of medication rather than medication adherence as a secondary outcome in our protocol (17). A nested qualitative study was conducted to explore the experiences of group participants and reasons for drop out from group treatment. A maximum variance sample (number of treatment sessions attended, sex, age, number of previous bipolar episodes, geographical location of

group) of participants received a single semi-structured digitally recorded interview on completion of group treatment at that site.

The SF-12 was added to the measures outlined in the protocol to measure physical health with the approval of the study Trial Steering Committee. The economic analysis, medication adherence and theoretical psychological measures of process will be separately reported.

Sample size.
Based on the first two RCTs of group psychoeducation versus group support with at least 12 month follow up (8,9), a differential treatment effect of 0.22 was estimated (60% recurrence in the control group, 38% in the psycho-education group at 12-months follow-up). As the study involved a group administered intervention, we adjusted the sample size for the clustering effect assuming a mean group size of 18 at randomisation, with an intra-cluster correlation (ICC) for group therapy of 0.05. Based on these assumptions a study with 360 service users (10 groups per arm) has power greater than 80% assuming 15% loss to follow-up. During the conduct of the RCT, the average group size was observed to be 14. With the agreement of the independent trial data monitoring committee, the numbers of groups per arm was increased and sample size was adjusted as a smaller group size reduces the effect of clustering. Assuming a mean groups size of 14, a trial with 308 participants (11 groups per arm) has 82% power.

Statistical and qualitative data analysis.
All analyses are intention to treat subject to the availability of data with a two sided type 1 error rate set at five per cent. Kaplan Meier curves and median time for first relapse are presented as summary statistics. A Cox model with robust standard errors to account for the therapy group effect was planned for the primary analysis. However, there was no clustering effect by therapy group for time to next bipolar episode, time to next mania episode or time to next depression episode so the standard Cox model results are presented. The proportional hazards assumption was checked by using log-log plots by arm alone and with additional covariates in the model. The treatment effect (PEd compared with PS) was adjusted for gender, number of previous bipolar episodes, and recruitment wave. We examined two pre-specified treatment moderators for the primary outcome: number of previous episodes (1-7, 8-19, >20 episodes minimised in the randomisation as part of the design) and participant treatment preference at baseline.

For continuous longitudinal data, the main statistical analysis used to compare the two interventions was a linear random effects model (LME) incorporating time as a continuous variable. Random effects were included to account for between-patient variation in the intercept and the gradient of the patient-specific lines. In addition, the models that also included random effects for wave and arm (nested within wave), to take account of therapy group clustering effects, were fitted. Fixed covariates were included to model systematic differences due to treatment, assessment time point and participant characteristics. Time since randomisation was calculated in months and was centred by subtracting the overall (grand) mean of assessment times for each outcome measure. Models included the fixed effect covariates: baseline measure, treatment group, centred time from randomisation to each assessment at 16-week intervals, the interaction between the baseline score and centred time in months, gender and number of previous bipolar episodes. In order that that all subjects with outcome data could be included in the LME analyses missing baseline response values were imputed using simple (deterministic) imputation (30). We estimated a time-treatment interaction (i.e., difference in slopes) and a main effect. Where the time-treatment interaction was not significant the main effect was estimated without the interaction term which is the difference between treatments averaged across

time. More detail of the analysis can be found in the Statistical Analysis Plan on line. All analyses were carried out using STATA Release 13.

Qualitative interviews were analysed using thematic analysis (31) taking an inductive and emergent approach based on participant's experiences of the groups. Coding was performed by a multidisciplinary panel (health and clinical psychology, psychiatry, service user) and subsequent interviews sought evidence to refute emerging themes. Themes were continuously compared against the data using a constant comparative approach. Interviews were conducted until themes were saturated.

Role of the funding source.

The funder of the study had no role in study design, data collection, data analysis, data interpretation or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results.

From September 2009 to June 2012, 304 participants were recruited, 153 to PEd and 151to PS. Figure 1 shows the flow of participants through the trial. Data on all bipolar relapses, mania and depression relapses were completed using primary care and secondary care records. Four participants (one PEd and 3 PS) died in the follow-up period of the study. Three died from natural causes and one from open verdict. The independent trial steering and data monitoring and ethics committees deemed these deaths to be unrelated to the interventions or procedures in the trial. Ten unblindings were reported (three PEd, seven PS) where the participant divulged their group allocation to their RA with subsequent follow up by another blinded RA. Six raters made 292 inter-rater reliability assessments of 17 subjects with a mean of 17.2 assessments of each subject and 2.35 assessments per time point. The ICC was 0.71 (95% CI 0.64 to 0.85) for depression scores and 0.57 (95% CI 0.40 to 0.83) for mania scores, indicating a high level of inter-rater agreement for depression symptoms but moderate for mania symptoms. Therapist and supervision records and qualitative interviews confirmed that PE sessions followed the manual and therapist led while PS followed topics decided by the participants and was peer led.

Table 1 shows the baseline characteristics by treatment group. Over half the participants had 20 or more previous bipolar episodes and most were taking mood stabilising medication and either antipsychotic drugs or antidepressants. Participants scored below the clinical threshold for significant depression, mania or anxiety symptoms and showed mild to moderate impairment in social adjustment at baseline (appendix, Tables A3 and A4). There were no significant differences in the demographic or clinical characteristics that were measured, between participants who self-referred or were referred by secondary care, nor between participants from different sites.

Table 2 shows attendance at treatment groups. The median attendance in PEd was 14 sessions (IQR 15.5) versus 9 sessions (IQR 15) in the PS group. Overall, attendance at PEd groups was greater than in the PS groups (Mann-Whitney test $z = 2.23$, $p = 0.026$).

Figure 2 shows the time to first bipolar episode (primary outcome measure). By 96 weeks, 89/153 (58%) PEd versus 98/151 (65%) PS participants had a first bipolar episode. The median time to first bipolar episode in PEd was 67 (95% CI 37 to 91) weeks after baseline versus 48 (95% CI 31 to 66) weeks in the PS groups. After adjustment for pre-specified covariates in a cox proportional hazards model there was no evidence from the primary analysis of an intervention effect (hazard ratio (HR)

0.83; 95% CI 0.62-1.11; p=0.217). Planned moderator analysis based on an interaction between treatment arm and number of previous bipolar episodes (1-7, 8-19 and 20+) indicated that, in those participants with 1-7 previous episodes, PEd may delay time to next bipolar episode compared to PS (appendix, Figure 2a) (χ^2 = 6.80, p=0.034). The subgroup specific hazard ratios of PEd compared to PS were 0.28 (95% CI 0.12 to 0.68) for 1-7 previous episodes, 0.86 (95% CI 0.50 to1.49) for 8-19 and 1.01 (95% CI 0.70 to 1.46) for 20 or more episodes. There was no evidence that participant treatment preference prior to randomisation had a moderating effect on time to first bipolar episode (χ^2 = 1.95, p=0.38).

Figure 3 suggests that the proportion of participants with a first mania-type episode was lower in PEd compared with PS (PEd: 39/153, 25%; PS: 53/151, 35%). In both treatment arms insufficient numbers of the participants relapsed to report the median time to relapse with 95% confidence intervals. The 25th centile of the time to episode was greater in the PEd arm (90 weeks) than the PS arm (53 weeks) but the upper 95% confidence interval is undefined. After adjustment for pre-specified covariates in a cox proportional hazards model there was some evidence that time to mania-type episode was longer for PEd as compared to PS (HR 0.66, 95% CI 0.44-1.002, p = 0.049). The difference between the PEd and PS groups in relation to time to mania episode appeared at around session 15 when early warning signs of mania were being discussed in PEd,

There was no evidence of differences in the time to first depressive episode (HR 0.96; 95% CI 0.70 to 1.31; p = 0.784). The proportion with a depressive episode between participants in the PEd arm (80/153; 52%) compared to those people allocated to PS (82/151; 54%). Again insufficient participants relapse to report the median time to relapse with confidence interval. The 25th percentile time to first depressive episode was 22.0 weeks (95% CI 15 to 29) in the PEd participants and 19 weeks after baseline (95% CI 15 to 28) in the PS group (Figure 4).

There were no significant effects on symptoms, or self-rated mental or physical health outcomes (appendix, Tables A3 and A4). Participants in PEd improved faster in the SAS interpersonal domain than in PS (difference in gradient -0.017, 95% CI -0.030 to -0.004, p = 0.012). There was no evidence of a treatment by time interaction for the remaining SOFAS and SAS (overall, friction and dependency) function outcomes (appendix Table A5). Full economic and medication adherence results will be reported elsewhere but there were no clinically important differences in the use of medication between the groups.

Qualitative data (appendix Tables A6 and A7) show the participants of both groups and the emerging themes. Two themes concerning the value of both groups emerged, "increased knowledge" in general about BD and specifically applied to them as an individual, and "people like me" tackling isolation and stigma, sharing similar experiences of having BD. Some participants related dropping out of treatment to the lack of structure of the PS groups.

Discussion.

The primary clinical results indicate that there was no significant difference on the primary clinical outcome of group psychoeducation (PEd) for BD versus group support (PS) on time to first bipolar episode after randomisation. Both groups provided general information about BD tailored to the participant, and provided emotional support beyond what can be provided in general written information recommended in NICE service user mental health guidelines (4). However there was evidence of some important benefits of PEd over PS and none for PS over PEd. There may be a

substantial delay in time to the next bipolar episode in people with seven or fewer previous bipolar episodes, while time to mania was delayed and interpersonal function improved faster for all participants. Attendance at PEd groups was better than at PS groups and the lack of structure was seen as a reason for dropping out of PS.

The strengths of the study are its large size, multicentre design, independence of the research team, pre-registration, allocation concealment, complete follow up on the primary outcome over two years, careful matching of therapists and duration of treatment, minimisation of patients across treatment arms for the natural history of the condition, few unblindings, training and supervision to ensure fidelity to treatment, and full reporting of clinical outcomes identified by NICE as being relevant to patients and clinicians (1, 16). Broad eligibility criteria and 22 groups at eight centres increased its generalisability.

Limitations of the study are the low rate of completion of self-rated symptomatic and functional limiting the certainty of the conclusions that can be drawn on these outcomes, moderate reliability of the assessment of mania symptoms, no formal rating of blinding, and the lack of recording of treatment sessions to absolutely ensure fidelity to treatment. However, none of these limitations are likely to change the main finding of no evidence of clinical benefit on delay of the next bipolar episode. A limitation of the trial design is that there is no treatment-as-usual control group with minimal information giving, although arguably such practice is now regarded as poor and not supported by NICE (1, 4). Given that the PS group included some approaches that may be components of effective psychological treatments for bipolar disorder such as problem solving (1, 32), PS may have been more effective than treatment as usual.

The results confirm a recent meta-analysis of RCTs on psychoeducation (14) that concluded the first RCTs of group psychoeducation versus group support (8,9) may be outliers in showing a much greater treatment effect versus control treatment than subsequent RCTs. Previous RCTs of group psychoeducation have been smaller single centre studies usually with shorter follow up, lack of blinding and complete reporting of all outcome measures, evaluated by the same investigators that developed the intervention, and without an optimised support group providing information and support tailored to the person with BD. When all of these methodological weaknesses are controlled then there is less evidence of clinical superiority of structured group psychoeducation versus unstructured group support. Thus the benefits of group psychoeducation are in the provision of information about BD from health professional and other service user perspectives and emotional support that reduce social isolation and stigma.

The large sample size and matching of participants by number of previous episodes allowed us to explore if there is an interaction between psychological treatment and number of previous bipolar episodes as some studies have previously shown (22, 33), but others have not (34). Number of previous bipolar episodes may be prone to recall bias and are not precise; however, a person with a few episodes can be distinguished readily from someone with 20 or more previous bipolar episodes. The current RCT demonstrated that in people with a few episodes (1-7), PEd may have been more effective than PS against time to next depression episode and time to next bipolar episode. The result requires replication in a sample confined to people early in the course of BD; RCTs of psychological interventions compared to treatment as usual confined to participants early in the course of their illness report clinical and cost effectiveness (35, 36). Previous RCTs of group psychoeducation versus group support may have shown a greater effect of group psychoeducation on time to the next bipolar episode than the current study because their sample recruited more participants in the early course of

their illness (8, 33). PEd may be more effective if early warning sign interventions are delivered earlier in the course because half the participants had dropped out by week 14 when these effective techniques (37, 38) were discussed and differences in time to mania relapse between the two groups start to emerge.

NICE guidelines for BD and other mental health conditions (1, 4) regard the provision of information and support as important outcomes in their own right but group psychoeducation is no more effective in terms of clinical outcome, except possibly on delay of mania episodes, than other less structured approaches. Group psychoeducation provides both general and tailored information and support from both health professional and service user perspectives at a relatively cheap price so it is an approach that may have merit in clinical practice, but not to the exclusion of other approaches that may deliver information and support of similar quality alongside other NICE recommended treatments for bipolar disorder such as medication (1). However, the optimised group support provided in this study is unavailable routinely in the United Kingdom in the precise form delivered in this RCT.

Although meta-analysis of previous RCTs suggests that group psychoeducation may increase time to relapse compared to treatment as usual, these RCTs were of low or very low quality so there remains some doubt requiring further research. Our results and the results of other recent psychological interventions (22, 33, 35, 36) suggest that the optimal provision of structured psychological interventions such as PEd early in the course of bipolar disorder may have important benefits on the course of illness, and merits further research.

4,940 words.

Funding.
This study was funded as part of the PARADES Programme Grant for Applied Research (RP-PG-0407-10389) by the National Institute for Health Research, Department of Health, England. It received further support from primary care trusts, mental health trusts, the Mental Health Research Network and Comprehensive Local Research Networks in the East Midlands and North West England. The views expressed by the authors do not necessarily reflect those of the National Institute for Health Research, the National Health Service nor the Department of Health in England.

Conflict of Interest.
None of the authors report any financial or personal conflict of interest.

Acknowledgements.
We would like to acknowledge the help and support of Bipolar UK, MIND and Mood Swings who all helped to publicise the study, Manchester Health and Social Care NHS Trust for hosting the PARADES programme, the University of Nottingham for providing sponsorship and clinical trials unit support for this trial, and the Spectrum Centre, University of Lancaster and University of Manchester for additional support. In particular we acknowledge the contributions of the following without whom the study would not have been possible: Ali Beck, Jelena Jovanoska, Natasha Lyon Karthik Thangavelu, Ayaz Quereshi, Kat Taylor, Ayesha Ahmed, Paul Hammersley, Brian Langshaw, Kathryn Reeveley, Kay Hampshire, Phil Byrne, Kiran Pindiprulu, Puru Pathy, Kirsten Nokling, Rachel Lambourne, Claire Hilton, Kirsty Stevenson, Rebecca Anderson,Dawn Knowles, Debbie Mayes, Lisa Brown, Dionysios Ntais, Elizabeth Camacho, Lizzie Tyler, Richard Pattison, Elly McGrath, Lorraine Getten, Emily Goodman-Smith, Lucy Bateman, Emma Weymouth, Lynda Fretwell, Sara Zarbakhsh, Mahesh Nachami, Sian Newman, Marcus Barker, Glyn Judge, Matthew

Impey, Steve Kendall, Sue Lomas, Jane Fisher, Nancy Black. We would also like to thank the participants in the study.

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